

What is claimed is:

1. A method of inhibiting the lethal effect of expressing an otherwise lethal protein in a cell, said method comprising:

- (a) providing a cell, tissue or organism having
  - (i) a nucleotide sequence encoding a Gas1 protein, or a functional equivalent, derivative or bioprecursor thereof, which is capable of inducing apoptosis in said cell and
  - (ii) a further nucleotide sequence encoding a protein which is otherwise lethal to said cell in itself or in response to a lethal stimulus in the presence of Gas1;
- (b) inhibiting function and/or expression of said Gas1 protein or functional equivalent, derivative or bioprecursor thereof; and
- (c) expressing said sequence encoding said otherwise lethal protein.

2. A method of identifying compounds which inhibit or enhance expression or activity of proteins which are lethal to a cell, tissue or organism said method comprising:

- (a) providing a cell, tissue or organism comprising a nucleotide sequence encoding a Gas1 protein or a functional equivalent, derivative or bioprecursor thereof, which is capable of inducing apoptosis in said cell, and ii) a further sequence encoding a protein which is otherwise lethal to said cell in itself or in response to a lethal stimulus in the presence of Gas1;
- (b) inhibiting function and/or expression of said Gas1 protein or functional equivalent,

derivative or bioprecursor thereof or a protein in the apoptotic pathway of which Gas1 is a component;

- (c) expressing said sequence encoding said otherwise lethal protein;
- (d) contacting said cell with a compound to be tested; and
- (e) monitoring the effect of said compound on said otherwise lethal protein compared to an identical cell which has not been contacted with said compound.

3. A method according to claim 1 or 2 wherein said expression or activity of Gas1 protein is inhibited by providing a nucleic acid molecule in said cell which is capable of hybridising to mRNA corresponding to Gas1 DNA to prevent expression thereof.

4. A method according to claim 1 or 2 wherein said expression or activity of said Gas1 protein is inhibited by inhibiting the expression or activity of a protein in the pathway of which Gas1 is a component.

5. A method according to any of claims 1 to 4 wherein said cell is induced to express said Gas1 protein by contacting said cell with a stimulus that increases intracellular calcium levels in said cell.

6. A method according to claim 5 wherein said cell is induced to express said Gas1 protein by contacting said cell with a suitable compound, such as muristerone.

7. A method according to any of claims 1 to 6 wherein said further sequence encoding said otherwise lethal protein is expressed by providing it on a suitable expression vector.

8. A method according to any of claims 1 to 7 wherein said lethal protein is a highly expressed recombinant protein.

9. A method according to any of claims 1 to 7 wherein said otherwise lethal protein comprises any of a glutamate, NMDA, AMPA or kainate receptor.

10. A method according to claim 9 wherein said glutamate receptors comprises any of a type 1 to 8 metabotropic receptor.

11. A method according to any of claims 3 to 9 wherein said nucleic acid molecule is provided as an oligonucleotide or as a vector including a nucleotide sequence of said nucleic acid molecule.

12. A method according to claim 11 wherein said nucleic acid molecule comprises an oligonucleotide consisting of the nucleotide sequence depicted in Sequence ID No. 5.

13. A method according to claim 11 wherein said nucleic acid molecule further comprises ribozyme or DNzyme activity.

14. A method according to any of claims 1 to 13 wherein said Gas1 protein is of mammalian origin.

15. A method according to claim 14 wherein said Gas1 protein is from any of a human, mouse or rat.

16. A method according to claim 14 or 15 wherein said Gas1 protein comprises the amino acid sequence depicted in either of Sequence ID No. 2 or 4 or a functional equivalent, derivative or bioprecursor thereof.

17. A compound identifiable as an inhibitor or an enhancer of expression or activity of an otherwise lethal protein according to the methods of any of claims 2 to 15.

18. A pharmaceutical composition comprising a compound according to claim 17 together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

19. A compound according to claim 17 for use as a medicament.

20. Use of a compound identifiable as an enhancer of expression or activity of a lethal protein according to claim 17 in the manufacture of a medicament for treating a disease condition mediated at least in part by underexpression or reduced activity of said otherwise lethal protein or a protein in the pathway of which said otherwise lethal protein is a component.

21. Use of a compound identifiable as an inhibitor of expression or activity of an otherwise lethal protein according to claim 17 in the manufacture of a medicament for treating a disease condition mediated at least in part by overexpression or reduced activity of said otherwise lethal protein

or a protein in the pathway of which said otherwise lethal protein is a component.

22. Use according to claim 20 or 21 wherein said disease condition comprises any of a neurological disorder, a cardiovascular disorder, an autoimmune disorder, a neuroendocrine disorder or cancer.

23. A method of monitoring the severity of a disease condition mediated by cellular apoptosis in a cell, tissue or organism comprising measuring the level of expression or activity of a Gas1 protein or a functional equivalent, derivative or bioprecursor thereof in said cell or tissue or organism.

24. A nucleic acid molecule encoding a rat Gas1 protein or a functional equivalent, derivative or bioprecursor thereof, comprising an amino acid sequence according to Sequence ID No. 2.

25. A nucleic acid molecule encoding a protein capable of inducing apoptosis in a cell comprising an amino acid sequence according to Sequence ID No. 4 or a nucleic acid molecule complementary thereto.

26. A nucleic acid molecule according to claim 24 or 25 which is a DNA sequence.

27. A nucleic acid molecule according to claim 26 which is a cDNA molecule.

28. A nucleic acid molecule according to claim 24, 26 or 27 comprising the sequence of nucleotides according to Sequence ID No. 1.

29. An antisense molecule capable of hybridising to the nucleic acid molecule of any of claims 24 to 28 under conditions of high stringency.

30. An antisense molecule according to claim 29 comprising a sequence of nucleotides according to Sequence ID No. 3 or 5.

31. A Gas1 protein encoded by a nucleic acid molecule according to any of claims 24 to 28.

32. A Gas1 protein comprising an amino acid sequence illustrated in Sequence ID No. 2.

33. A protein capable of inducing apoptosis in a cell comprising an amino acid sequence according to Sequence ID No. 4 or a functional equivalent, derivative or bioprecursor thereof.

34. An expression vector comprising a nucleic acid molecule according to any of claims 24 to 28.

35. An expression vector according to claim 34 wherein said vector is any of a plasmid, virus or phage derived vector.

36. An expression vector according to claim 34 or 35 comprising a tissue or cell specific promoter.

37. An expression vector according to any of claims 34 to 36 further comprising a sequence encoding a proapoptotic protein.

38. An expression vector according to any of claims 34 to 37 which is inducible for expression of

said Gas1 polypeptide or said polypeptide capable of inducing apoptosis in a cell.

39. An expression vector according to claim 38 comprising the inducible vector pIND.

40. A host cell, tissue or organism, transformed, transfected or infected with a vector according to any of claims 34 to 39.

41. A method of identifying compounds capable of preventing or accelerating Gas1 mediated cell death comprising the steps of:

- (a) contacting a cell, tissue or organism expressing Gas1 or a functional equivalent, derivative or bioprecursor thereof capable of inducing apoptosis in a cell with said compound to be tested; and
- (b) monitoring the effect of said compound on the state of said cell compared to a cell which has not been contacted with said compound.

42. A method according to claim 41 wherein said cell in step (a) comprises a cell according to claim 40.

43. A compound identifiable as an inhibitor or an accelerator of cell death according to the method of claim 41 or 42.

44. A pharmaceutical composition comprising a compound according to claim 43, together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

45. A pharmaceutical composition comprising any of a nucleic acid molecule according to any of claims 24 to 28, an antisense molecule according to claim 29 or 30, a protein according to any of claims 31 to 33 together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

46. Use of any of a nucleic acid molecule according to any of claims 24 to 28, an antisense molecule according to claim 29 or 30, a protein according to any of claims 31 to 33, a compound according to claim 43 or a pharmaceutical composition according to claim 44, in the manufacture of a medicament for the prevention or treatment of a disease condition mediated at least in part by expression of a Gas1 protein or a functional equivalent, derivative or bioprecursor thereof capable of inducing apoptosis in a cell or a protein in the pathway of which Gas1 is a component.

47. Use according to claim 46 wherein said disease condition is any of a neurological disorder, a cardiovascular disorder, an autoimmune disorder, a neuroendocrine disorder or an oncological disorder.

48. Use according to claim 47, wherein said neurological disorder is any of, Parkinson=s disease, Alzheimer=s disease, Huntington=s disease, amyotrophic lateral sclerosis, a neurological condition caused by thrombosis or cerebral trauma.

49. Use according to claim 47, where said cardiovascular disorder is a heart attack.



50. Use according to claim 47, wherein said autoimmune disorder is multiple sclerosis.

51. Use according to claim 47, wherein said neuroendocrine disorder is necrosis of the pituitary gland.

52. An antibody capable of binding to a protein according to any of claims 31 to 33.

53. A pharmaceutical composition comprising an antibody according to claim 52 together with a pharmaceutically acceptable carrier, diluent or excipient therefor.